Correspondence

COVID-19 vaccines do not trigger psoriasis flares in patients with psoriasis treated with apremilast

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Dear Editor,

Although COVID-19 vaccination is strongly recommended for patients with psoriasis (PsO) by several dermatological societies worldwide, only one recently published Italian case series has reported the safe and effective role of the vaccine in this patient subset. Notably, the vaccine information highlights that there are limited data about the vaccine in immunosuppressed patients and that vaccination should be performed in agreement with the vaccinator.[1] Furthermore, PsO itself is not considered an immunosuppressive status, but some antipsoriatic, effective and safe drugs are codified as immunosuppressants. Thus, patients with moderate to severe PsO undergoing targeted therapies [e.g. interleukin (IL)-17 inhibitor (i), IL-12/23i, IL-23i and tumour necrosis factor-α], small molecule therapy (apremilast, dimethyl fumarate) and conventional therapies (methotrexate, ciclosporin) are considered immunosuppressed by the World Health Organization.[2] Among the systemic antipsoriatic treatments, only acitretin is not considered an immunosuppressant (Table 1).

Apremilast, a phosphodiesterase (PDE)-4 inhibitor, displays immunomodulatory effects on both keratinocytes and immune cells, decreasing cutaneous hyperplasia and mitigating the proinflammatory microenvironment. Notably, apremilast is orally delivered and well-tolerated in young patients, needlephobics and patients with other circumstances that represent a relative contraindication for biologics (e.g. neoplasia or HIV).[2] For some patients with PsO, the COVID-19 pandemic has affected adherence,[3] anti-vaccination opinions[4] and lifestyle,[4] complicating the monitoring of chronic immunosuppressive therapy. There are no data on interactions between apremilast and COVID-19 vaccines to guide physician daily practice during the ongoing pandemic. We report three patients with PsO under apremilast who also received COVID-19 vaccination.

Patient 1 was a 48-year-old man with PsO and psoriatic arthritis (PsA). Following nonresponse to ixekizumab or etanercept, the patient was commenced on apremilast, achieving stable remission, which was maintained for 8 months. He experienced flares of both his PsO and PsA during asymptomatic COVID-19, which resolved spontaneously 10 days after COVID-19 remission. Six months after this infection, he received both doses of the Pfizer mRNABNT162b2 vaccine without experiencing any PsO flare.

Patient 2, a 76-year-old man with PsO, had been taking apremilast since 2017 with a stable residual Psoriasis Area Severity Index (PASI) of 3. After the first dose of the AstraZeneca-Oxford vaccine AZD1222 he experienced fever (38.5 °C) and myalgia for 3 days, whereas the second dose was not complicated by any adverse effects (AEs). On both occasions he did not experience any PsO flare.

Table 1 The Anatomical Therapeutic Chemical Classification System for the main systemic antipsoriatic drugs published by the World Health Organization Collaborating Centre for Drug Statistics[a] Methodology.

	ATC five-levels code					
Systemic drug	I[b]	II[c]	III[d]	IV[e]	V[f]	IS
Conventional therapies						
Methotrexate	L	04	A	X	03	Yes
Ciclosporin	L	04	A	D	01	Yes
Acitretin	D	05	B	B	02	Not
Small molecules						
Apremilast	L	04	A	A	32	Yes
DMF	L	04	A	X	03	Yes
Biologics						
Etanercept[g]	L	04	A	B	01	Yes
Infliximab[g]	L	04	A	B	02	Yes
Certolizumab	L	04	A	B	05	Yes
Adalimumab[g]	L	04	A	B	04	Yes
Ustekinumab	L	04	A	C	05	Yes
Secukinumab	L	04	A	C	10	Yes
Ixekizumab	L	04	A	C	13	Yes
Brodalumab	L	04	A	C	12	Yes
Guselkumab	L	04	A	C	16	Yes
Tildrakizumab	L	04	A	C	17	Yes
Risankizumab	L	04	A	C	18	Yes

ATC, Anatomical Therapeutic Chemical Classification System; DMF, dimethyl fumarate; IS, immunosuppressant. [a]https://www.whocc.no/atc_ddd_index/; [b]one letter that indicates the anatomical main group among the 14 codified; [c]two digits that indicate the therapeutic subgroup; [d]one letter that indicates the therapeutic/pharmacological subgroup; [e]one letter that indicates the chemical/therapeutic/pharmacological subgroup; [f]two digits that indicate the chemical substance; [g]includes its biosimilars.

Patient 3 was a 36-year-old woman with plaque PsO (PASI 3) and concurrent pustular PsO (Palmoplantar Psoriasis Area and Severity Index 2.3), who had been stably treated with apremilast and narrowband UVB for 3 years. She received the Pfizer mRNABNT162b2 vaccine without any AEs or PsO flare.

All four patients developed IgG antibodies to the SARS-CoV-2 S1 receptor binding domain, suggesting that apremilast does not interfere with the acquisition of SARS-CoV-2 immunity. Furthermore, none of the COVID-19 vaccines, both mRNA-based and viral vector-based, did not trigger PsO or PsA flares in any of these three patients treated with apremilast. Interestingly, real-life data have also highlighted the potential protective effect against SARS-CoV-2 in this patient subset,[5,6] while at the same time warning about the possible apremilast-related gastrointestinal and taste AEs, which may be misinterpreted as suggestive of COVID-19.[7–9]

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